REMARKS

Claims 1-17, 47 and 48 are pending in the case and all have been rejected.

Claim Objections

Claims 2, 4-8, 10 and 48 were objected to due to the inclusion of non-elected subject matter in that they cover sequences in addition to those elected for examination of the combination claims of Group I. In response, claim 2 has been amended to recite the 10 sequences previously elected (SEQ ID NO: 110, 653, 683, 767, 804, 820, 910, 1019, 1040 and 1247).

Claim 15 was objected to for use of the phrase "of one of claim 1" and this claim has now been amended to correct this matter.

Rejection Under 35 U.S.C. §112 (First Paragraph)

Claims 1-17, 47 and 48 were rejected under 35 U.S.C. 112, first paragraph, as failing to meet the written description requirement due to open claim language such as "containing a gene that corresponds to a polynucleotide" (claim 1) and "comprising a nucleotide sequence corresponding to a gene" (claim 54). Applicant initially notes that there is no claim 54 and believes that the Examiner meant claim 48.

Applicant also responds that this cannot be based solely on use of open ended language because such language as "comprising" is standard claim language and such a rejection could therefor be applied to almost every patent claim. Thus, this rejection must be predicated on use of the term "corresponding" in conjunction with "comprising."

In response, Applicant directs the Examiner's attention to the application starting at page 11, line 29, where the term "correspond" is defined as meaning a gene that encodes an RNA at least 90% identical to the claimed polynucleotide, which could include an RNA pre- or post-processing (see application at page 12, lines 14-28). In essence, the term "correspond" is intended to indicate polynucleotides that encode substantially the same RNA as a gene in a cell because the disclosed polynucleotides of the application are cDNAs while the genes contained in cells used for the screening process of claim 1 will commonly be genomic sequences contained in cancerous or normal cells as recited in the claim (or may be cDNAs transfected into recombinant cells used for screening). For example, such polynucleotides would encode the same protein as the gene it corresponds to in the case where the gene encodes a protein (see application at page 13, lines 9-17).

In addition, Applicants note that the methods of claims 1 and 48 relate to contacting a cell with a test compound to be evaluated for gene modulating ability. The gene to be modulated is therefor contained in the cell used in the screen and such gene may certainly be part of the genome of said cell, in which case it will be part of a larger polynucleotide structure. Thus, the cell comprises the gene, which gene corresponds to the polynucleotide recited in the sequences.

Further, the sequences disclosed by Applicants are mostly cDNA sequences so that they result from processed RNA species from which intronic sequences may have been removed as a result of intracellular processing. For this reason it would avail Applicants little to identify the gene as comprising one of the disclosed sequences since such cDNA sequence, as such, may not be contained within the cell (except in the case of a recombinant cell wherein the cDNA represents the heterologous gene). In addition, gene expression is normally determined by measuring RNA expression and the structure of the RNA therefor "corresponds" to both the gene expressing it as well as the cDNA that would be formed from it. Consequently, the gene of the cell and the polynucleotide disclosed by Applicants correspond to each other through the RNA that is related to both.

As a result, Applicants define the term "correspond" as in the application starting at page 11, line 29, as meaning a gene that encodes an RNA at least 90% identical to the claimed polynucleotide, which is commonly a cDNA sequence, and could include an RNA pre- or post-processing (as stated in the application at page 12, lines 14-28).

In sum, a user of a method of the invention may well use a cell that contains the genomic counterpart of a polynucleotide (such as a cDNA sequence) disclosed by Applicants and thus it would be expression of the genomic counterpart of Applicant's polynucleotide that is being measured. However, such would readily be recognized by those skilled in the art and therefor in no way detracts from the patentability of the invention as recited in claims 1 and 48 (and claims dependent therefrom).

In view of the foregoing, Applicants believe that the written description requirement has been met by the application disclosure as filed and thus claims 1 and 48, and claims dependent therefrom, should be allowed.

Rejection Under 35 U.S.C. §112 (Second Paragraph)

Claims 1-17, 47 and 48 were rejected as vague and indefinite. Claims 1 and 48 were rejected for use of the term "corresponds" and "corresponding." In response, Applicant urges that the above-recited arguments regarding written description are equally applicable here and that this ground of rejection should be withdrawn.

Claim 48 was rejected as vague for use of the phrase "a polynucleotide comprising a nucleotide sequence corresponding to a gene." Applicants respond by reiterating the above-description of the term "correspond" and note that the indicated phrase merely refers to the fact that the polynucleotide used for screening is contained in a cell as recited in the claim and therefore may be part of the genome of the cell, thus being part of a larger polynucleotide structure. Thus the cell would contain a gene capable of

modulation and the sequence of the gene would correspond to one of the polynucleotides disclosed in the application as exhibiting increased expression in a cancerous versus a non-cancerous cell or vice versa (for example, as based on RNA levels). Applicants believe that this recitation is sufficiently clear to avoid any argument for vagueness.

Claims 1 and 48 were rejected as indefinite for use of the terms increase and decrease and elevated. Applicants note that the application indicates the observed changes in expression for the different ranges of SEQ ID NOs disclosed in the application. Further, applicants believe that those skilled in the art are well capable of determining whether a change in gene expression due to the presence of a potential therapeutic agent is reliable, and useful, or not. Applicants also note that the invention is directed to determining the effects of chemical agents on the expression of more than one genes in cancerous versus non-cancerous cells or vice versa and that it is the overall profile of gene modulation that is relied on in determining the agent in question and not the absolute change in expression of any particular gene.

Claims 1 and 48 were also rejected as indefinite for use of the phrase "cancerous cell over that in a non-cancerous cell" etc. In response, Applicants have amended the claims to recite that the cells are from the same tissue type. This amendment is supported in the application, for example at page 21, lines 4-14.

Rejection Under 35 U.S.C. §102

Claims 1-17, 47 and 48 were rejected under 35 U.S.C. 102(e) as anticipated by Young et al (WO 01/94629).

In response, Applicants contend that Young et al does not meet the requirements of 102(e) as a reference as of its filing date because it does not designate

the United States as a designated state (see face page of the published application of Young et al).

In view of the foregoing, Applicants believe that this ground of rejection has been overcome.

Rejection Under 35 U.S.C. §103(a)

Claims 1-17, 47 and 48 were rejected under 35 U.S.C. §103(a) as being unpatentable over Robinson et al. (Pat. No. 6,232,065) in view of a number of GenBank Accession Nos., Young et al. (WO 01/94629) and Kinzler et al. (Pat. No. 5,702, 903).

Robinson et al. is offered as a basis of rejection on grounds that this patent discloses methods and compositions for screening factors that affect the expression patterns of individual genes or groups of genes in various disease states, including colon cancer, and also examining an entire gene family profile to identify important marker genes for subsequent experiments to identify cancer and other cancer-related testing. In addition, Robinson et al is cited as describing many of the multiple genes showing expression changes in a particular tyrosine kinase gene family. However, the Examiner concedes that Robinson et al do not describe a decrease in neoplastic activity due to cell death or the particular sequences disclosed by Applicants.

The Examiner attempts to make up for the latter deficiencies by relying on Young et al. However, because of the effective date of Young et al (i.e., its publication date rather than its filing date) as well as the other comments already made by Applicants, this reference has been removed and will thus not be described further.

The Examiner also relies on Kinzler et al to bolster the case for obviousness. This reference is relied on to show elevated gene expression in various tumors, such as those

from stomach, lung and colorectal cancer, as well as describing elevated expression over that normally produced in non-cancerous cells.

In response, Applicants urge that Kinzler et al merely use the normal cells to establish baseline expression levels (see Kinzler at column 5, lines 60-63). However, there is no mention of the sequences disclosed by Applicants as being involved in the cancerous process. The sequences and genes disclosed by Applicants herein were not previously known as being involved in the cancerous process, especially not when taken as a group or family (such as the signature gene sets disclosed by Applicants). It is the identity of the sequences in conjunction with their differential expression as a group (or, at least, as more than one gene) and uses thereof that forms a basis for the present invention. The mere fact that the sequences were previously known or that someone skilled in the art had previously disclosed use of differential expression of a gene for screening potential therapeutic agents in no way negatives patentability of the present invention.

At best, Kinzler et al. and Robinson et al. taken together merely tell those in the art to go out and look for genes and/or groups of genes. However, they do not render obvious the Applicant's claimed method since this involves specific sequences found by the Applicant as part of a larger profile.

The Examiner further relies on Robinson et al as teaching the monitoring of gene expression profiles resulting from cellular and physiological changes that can then be characterized for individual genes or groups of genes. Robinson further states that the invention can be used to screen drug compounds that affect biological samples and that human cancer is a result of genetic changes that result in alterations in the profile of expressed genes. The Examiner suggests that this method could be applied by combining the disclosures of Young et al and Kinzler et al to check for the presence of gene expression alterations involved in normal and cancerous tissue in order to find compounds that alter the differential expression between cancerous and non-cancerous

cells.

In response Applicants contend that these references, if combined, do not achieve the invention of the application. The Applicants concede that all of their disclosed sequences were already known in the art but not as being up-regulated in cancerous versus non-cancerous cells or vice versa. The Examiner cites accession numbers and references for sequences with high similarity or identity to 10 of the sequences disclosed by Applicant.

None of the references appear to recite use of genes elevated in normal cells as opposed to cancer cells although this is within the scope of claim 1 and is specifically required by claim 47. For example, Kinzler et al. uses non-cancerous cells to develop a baseline for elevated gene expression in cancerous cells but does not assess elevated production in normal cells versus cancerous cells (see Kinzler et al. at column 5, lines 60-67). In fact, several of the gene sequences provided by Applicant in the selected 10 sequences are elevated in normal over cancerous cells (for example, SEQ ID NO: 110 is expressed in cancer and not normal tissues of breast while SEQ ID NO: 653 is expressed in normal tissue but not ductal carcinoma of breast.

Applicant believes that this is an application of the "obvious to try" standard, which is not sufficient to show prima facie obviousness. (See, for example, In re Eli Lilly & C., 14 USPQ2d 1741, at 1743 (Fed. Cir. 1990), where this is defined as a general disclosure that "may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued.") In the present case, Applicant does not believe that a mention of finding a gene with differential expression in a cancer cell tells those skilled in the art to look for families of such genes, or determined expression profiles of such families, or to examine elevated expression in normal over cancerous cells or the particular sequences disclosed by Applicant (especially since Young et al is not a reference).

Additional Claim Amendments

In addition, claim 2 has been amended to be limited to use only of the sequences elected by Applicant.

Claim 11 has been amended to recite use of at least 3 said genes. Support for this amendment is found in the application at page 10, line 7.

Claim 14 has been amended to recite use of more than 10 said genes. Support for this amendment is found in the application at page 10, line 9.

Further, claim 47 was amended to recite the method of claim 1 wherein at least one gene is a gene elevated in cancer and not in normal cells and at least one gene is elevated in normal cells and not in cancer cells. For example, genes corresponding to some of the 10 sequences previously elected have been found to be expressed in normal but not cancer cells while genes corresponding to others of the selected sequences are expressed in cancer cells but not normal cells.

Applicant has included herewith a request for a 1 month extension of time and a check to cover the fee for a small entity. The Commissioner is authorized to charge payment of any fees required for filing this response, or credit any overpayment, to Deposit Account No. 03-0678.

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Respectfully submitted,

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